

**Notice of Allowability****Application No.**

09/589,589

**Applicant(s)**

HIGH ET AL.

**Examiner**

ANOOP SINGH

**Art Unit**

1632

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 2/1/2011.
2. ☒ The allowed claim(s) is/are 1,2,28 and 44.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some\* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08),  
Paper No./Mail Date \_\_\_\_
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☒ Interview Summary (PTO-413),  
Paper No./Mail Date 4/19/2011.
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other \_\_\_\_.

/Anoop Singh/  
Primary Examiner, Art Unit 1632

### **DETAILED ACTION**

Applicant's amendments and response filed February 1, 2011 have been received and entered. Claims 3-27, 29-42 have been canceled, while claim 1 has been amended. Claims 1-2, 28, 43 and 44 are pending and under consideration in the instant application.

The amendment to the specification filed April 20, 2010 has been entered.

The replacement drawings filed on December 10, 2002 have been entered.

#### ***Withdrawn-Claim Rejections - 35 USC § 103***

Claims 1-2, 28, 43 and 44 were rejected under 35 U.S.C. 103(a) as being unpatentable over Wilson et al (US Patent no 6,251,957, dated 6/26/2001, art of record), Conti-Fine (US 6,929,796, dated 8/16/2005, filed on 12/16/1997, art of record) and Nilsson et al (Proc. Natl. Acad. Sol. USA: 1986, 83, 9169-9173). Applicants' cancellation of claim 24 renders its rejections moot. In view of Examiners' amendments to the base claim presented in this office action obviates the basis of the rejection. It is noted that prior art teaches immunosuppressive agents particularly cyclophosphamide alone either failed completely, caused unacceptable adverse side effects, or was ineffective in preventing inhibitory antibodies to Factor IX (see Nilsson et al PNAS, 1986, 83, 9169, IDS and applicants' arguments filed on 10/26/2006 and 06/11/2007). Thus, rejection of claims 1-2, 28, 43 and 44 are hereby withdrawn in view of Examiner's amendments to the claims presented in this office action.

### **EXAMINER'S AMENDMENT**

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Kathleen Rigaut on September 22, 2011.

The application has been amended as follows:

***In the Specification***

On page 5, line 16, the terms "Figures 4A-4D" has been replaced with -- Figures 4A-4E --.

***In the claims***

Claim 43 has been canceled.

Following claims have been re-written as follows.

1. A method of preventing the formation of inhibitory antibodies to Factor IX delivered to a mammal by way of an adeno-associated viral vector, said mammal showing symptoms of hemophilia B and having a genetic defect which can result in generation of inhibitory antibodies to Factor IX upon administration of exogenous Factor IX, said method comprising

(a) intravenously or intraperitoneally administering to said mammal an immunosuppressant consisting of cyclophosphamide, and

(b) delivering Factor IX to said mammal by way of an adeno-associated viral vector, either concomitantly with or following step (a),

wherein the delivered Factor IX is from the same species as said mammal.

2. The method of claim 1, wherein said mammal is human.

44. The method of claim 1, wherein said adeno-associated viral vector is delivered intramuscularly.

Claims 1-2, 28 and 44 are allowed.

### *Conclusion*

The following is an examiner's statement of reasons for allowance: The instant specification is the first to show preventing formation of inhibitory antibodies to Factor IX delivered to a mammal by way of an AAV gene therapy by administering to the mammal cyclophosphamide alone. It is noted that closest prior art summarized by the references of Nilsson et al (Proc. Natl. Acad. Sol. USA: 1986, 83, 9169-91730) teaches away from using cyclophosphamide alone because cyclophosphamide alone was ineffective in preventing the formation of inhibitory antibodies to Factor IX.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANOOP SINGH whose telephone number is (571)272-3306. The examiner can normally be reached on 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272- 4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anoop Singh/  
Primary Examiner, Art Unit 1632